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December 19, 2003

"Subscribed and sworn to before me this 19th day of December, 2003"

Eugene J. Joseph Jr.
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Issued in Paris on Oct. 8, 2003

For the Executive Director of the
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The Head of the Patent Department

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1 NAME AND ADDRESS OF APPLICANT OR AGENT TO WHOM CORRESPONDENCE SHOULD BE SENT

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8142	ETL/an	01.53.77.44.78

2 APPLICATION Type of industrial property

☒ patent of invention ☐ divisional application ☐ initial application
☐ utility certificate ☐ conversion of a European patent application
☐ patent of invention ☐ utility certificate no. date

Preparation of search report ☐ deferred ☒ immediate

Is the applicant (if an individual) requesting an installment plan for the fee ☐ yes ☐ no

Title of the invention (200 characters of less)

Heteroaryl oxypropanolamines, process for their preparation and pharmaceutical compounds containing them

3. APPLICANT(S) SIREN No. APE-NAF Code

Last name and first name (underline last name) or d.b.a.

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Business corporation

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If insufficient space, continue on a separate sheet ☐

4. INVENTOR(S) Are the inventors the applicants ☐ yes ☒ no If not, provide separate inventor designation.

5. REDUCED FEE ☐ requested for the first time ☐ requested prior to filing; attach copy of approval

6. DECLARATION OF PRIORITY OR REQUEST TO USE THE FILING DATE OF A PRIOR APPLICATION

country of origin	number	filing date	type of application

7. DIVISIONS prior to this application no. date no. date

8. SIGNATURE OF APPLICANT OR AGENT
(name and title)
[signature]
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SIGNATURE OF EMPLOYEE ON RECEIPT

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9911204

TITLE OF THE INVENTION

Heteroaryl oxypropanolamines, process for their preparation and pharmaceutical compounds containing them

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Date and signature(s) of applicant(s) or agent Paris, September 10, 1999

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E. THOURET-LEMAÎTRE

[illegible]

This invention relates to new propanolamines, the pharmaceutical compounds that contain them, a process for their preparation, and intermediates in said process.

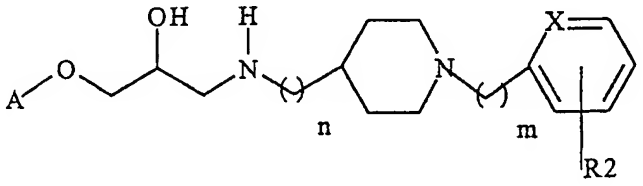
These new compounds have shown agonist activity with respect to the β_3 receptor and, therefore, may be used in the treatment of diseases that benefit from activation of this receptor.

BE 902897 describes aryl propanolamines that carry a 1-substituted 4-piperidinyl group on the amine, these compounds having β_1-blocking or α-blocking activity.

J. Org. Chem., 1988, 63: 889-894 describes other aryl oxypropanolamines that carry a 1-substituted 4-piperidinyl group on the amine.

It has now been found that heteroaryl oxypropanolamines that carry a piperidin-4-yl radical or piperidin-4-yl alkylene on the amine, possessing agonist activity with respect to β_3-adrenergic receptors.

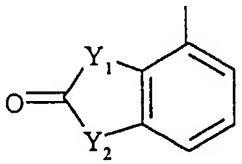
Thus, in one of its aspects, this invention relates to formula (I) propanolamines



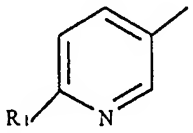
(I)

where X is N or CH;

A represents a group with formula (a) or (b)



(a)



(b)

R_1 represents hydrogen or a $-NH_2$, $-NR_3R_4$, $-NR_3CO(C_1-C_4)$ $Alk_5-NR_3SO_2(C_1-C_4)Alk$ group;

R_2 represents hydrogen or a $(C_1-C_4)Alk$ group, a (C_1-C_4)alkoxyl group, a halogen, $-COOH$, $-COO(C_1-C_4)Alk$, $-CN$, $-CONR_3R_4$, $-NO_2$, $-SO_2NR_3R_4$, $-NHSO_2(C_1-C_4)Alk$;

m and n independently represent 0, 1, or 2;

R_3 and R_4 independently represent hydrogen or a $(C_1-C_4)Alk$ group;

Y_1 and Y_2 independently represent NH or O;

and their salts or solvates.

In this invention, the term "(C_1-C_4)Alk" indicates a monovalent radical of a straight or branched chain, saturated C_1-C_4 hydrocarbon.

The salts of formula (I) compounds according to this invention include additive salts with pharmaceutically acceptable inorganic or organic acids such as hydrochloride, hydrobromide, sulfate, bisulfate, monobasic, citrate, maleate, tartrate, fumarate, gluconate, methane sulfonate, 2-naphthalene sulfonate, etc., as well as additive salts that allow adequate separation or crystallization of formula (I) compounds, such as picrate, oxalate, or additive salts with optically active acids, e.g., camphor sulfonic acid and mandelic acids or substituted mandelic acids.

In addition, when the formula (I) compounds have a free carboxy group, the salts also include salts with inorganic bases, preferably salts obtained with alkaline metal bases, such as sodium or potassium, or with organic bases.

Optically pure stereoisomers as well as mixtures of isomers of formula (I) compounds are part of this invention.

Preferred compounds of this invention include formula (I) compounds where X represents CH.

Other preferred compounds of this invention are those where X represents nitrogen and the R_2 group is in position 5.

Other preferred compounds are those where the (C_1-C_4)Alk group is a methyl or ethyl group.

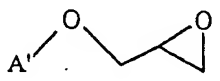
Other preferred compounds are those where the R_2 is one of the following: -COOH, -COO(C_1-C_4)Alk, -CN, NO_2, -CONR$_3$R$_4$, -NHSO$_2$-(C_1-C_4)Alk, Cl.

Still other preferred compounds are those where n and m are zero.

A particularly advantageous compound is 3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[1,2-dihydro-2-oxo-benzimidazol-4-yloxy]-2]-propanol (possibly salted).

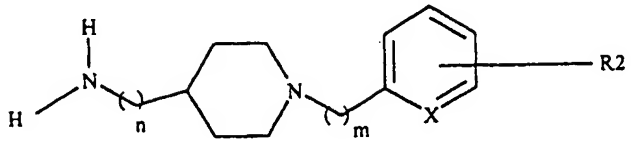
Another particularly advantageous compound is 3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[2-amino-pyrid-5-yloxy]-2-propanol (possibly salted).

The formula (I) compounds are prepared by processing a formula (II) epoxy:



(II)

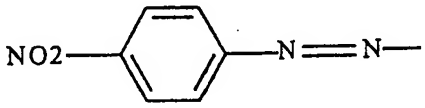
where A' represents the (a) group or the (b) group, in which R_1 is possibly protected by a protective group, with a formula (III) amine:



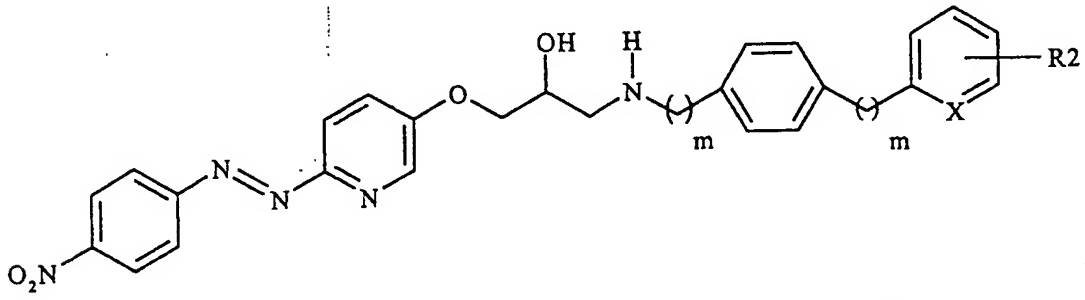
(III)

where m, n, R_2, and X are as indicated above, while eliminating the protective group that is possibly present and transforming the formula (I) product thus obtained into one of its salts or solvates.

Alternatively, when A represents a (b) group and R_1 is an NH_2 group, formula (I) compounds are preferably prepared by condensation of a formula (III) amine with a formula (II) product, where A' is the (b) group and R_1 is a group with the formula:



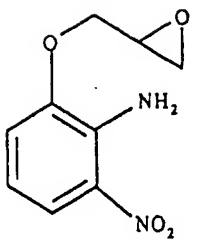
and by subjecting the formula (IV) product thus obtained:



(IV)

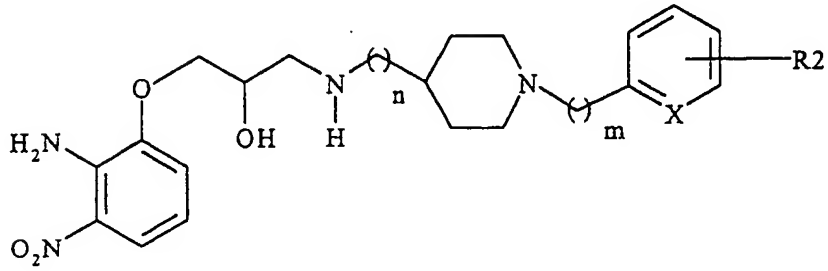
to a hydrogenation reaction to transform the 4-nitrophenyldiazenyle group into an amino group.

When A is a formula (a) group and Y_1 and Y_2 represent a nitrogen atom, it is also possible to prepare formula (I) compounds by processing a formula (V) compound:



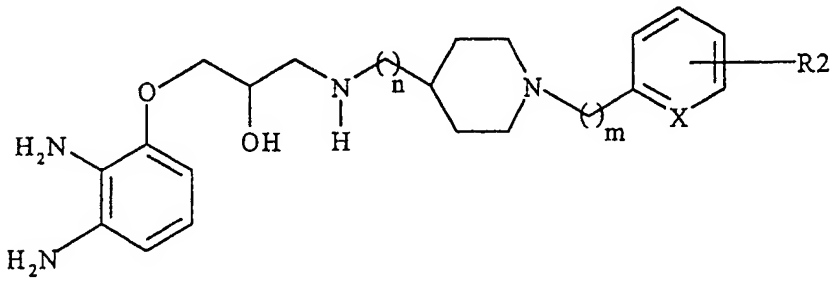
(V)

with a formula (III) amine, by reducing the nitro group of the formula (VI) product thus obtained:



(VI)

and processing the formula (VII) product thus obtained:



(VII)

with a carbonylation agent capable of inserting a carbonyl group into the molecule, such as carbonyl diimidazole or carbonyl chloride, to obtain the final product, which may be transformed into one of its salts or solvates.

The reduction of the nitro group to an amino derivative may be done, for example, by catalytic hydrogenation. As the reaction solvent, it is possible to use, for example, a polar protic solvent such as water or acetic acid, an acid such as ethanol, methanol, or isopropanol, an ester such as ethyl acetate, a linear or cyclic ether such as tetrahydrofuran or dioxane, or an aromatic solvent such as benzene or toluene.

The cyclization reaction is preferably done using carbonyl diimidazole in an inert solvent such as tetrahydrofuran or a linear ether, at a temperature between ambient temperature and the reflux

temperature of the selected solvent.

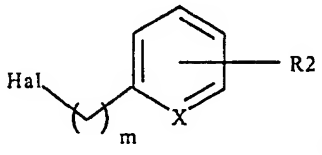
The reaction between the epoxies and the amine (III) is done in an organic solvent such as an inferior alcohol, e.g., methanol, ethanol, or isopropanol; dimethyl sulfoxide; a linear or cyclic ether; an amide such as dimethyl formamide or dimethyl acetamide, using at least equimolar quantities of the reagents, possibly with a slight excess of amine.

The reaction temperature is between ambient temperature and the reflux temperature of the selected solvent.

The formula (II) compounds where A' is an (a) group may be prepared according to the general process described in diagram III of WO97/10825 or according to patent DE 2700193.

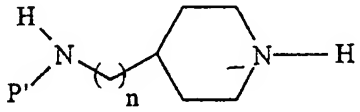
The formula (II) compounds where A' is a (b) group may be prepared according to the general process described in EP 0 611 003.

The formula (III) amines may be prepared by reaction of the appropriate synthons from formula (VIII):



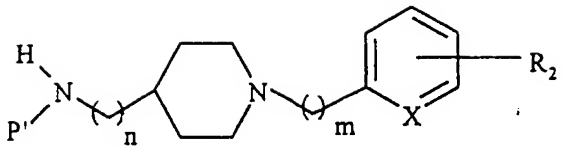
(VIII)

where Hal represents a halogen and R_2, m, and X are as specified above, with a piperidine from formula (IX):



(IX)

where n is as specified above and P' represents a protective group, in an organic solvent, in the presence of a base, followed by elimination of the P' group of formula (X) compounds thus obtained:



(X)

As a reaction solvent, for example, the following may be used: dimethyl formamide, pyridine, dimethyl sulfoxide, a linear or cyclic ether, or a chlorinated solvent such as dichloromethane.

As a base, for example, the following may be used: an alkaline hydroxide, an alkaline carbonate such as potassium carbonate, or a tertiary amine such as triethylamine.

The above condensation reaction is complete in several hours, normally in 2-12 hours.

The reaction temperature is between ambient temperature and the reflux temperature of the selected solvent.

As protective groups P', the following may be used: acyl groups such as formyl, acetyl, propionyl, phenoxyacetyl, etc.; an alkoxycarbonyl group such as tert-butoxycarbonyl, etc.; an alcoxycarbonyl group such as methoxypropionyl, etc.; a substituted alkoxycarbonyl group such as monochloromethylcarbonyl, dichloromethylcarbonyl, trichloromethylcarbonyl, trichloroethylcarbonyl, trichloropropylcarbonyl, trifluoromethylcarbonyl, etc.; a substituted arylalkoxycarbonyl group such as 4-nitrobenzyloxycarbonyl, etc.; a benzyl group; a substituted benzyl group; a diphenylmethyl group (possibly substituted); a trityl group (possibly substituted) such as 4-methoxyphenyldiphenylmethyl or di-(4-methoxyphenyl)phenylmethyl; a silyl group such as trimethylsilyl or ethyldimethylsilyl or tert-butyldimethylsilyl, etc.

Said protective groups may be eliminated using conventional methods, e.g., reduction or hydrolysis. A more detailed description of these amino-protective groups as well as methods for their preparation and elimination are given, for example, by T.W. Greene, "Protective Groups in Organic Synthesis," John Wiley & Sons, 1981, and by J.F.W. McOmie, "Protective Groups in Organic Chemistry," Plenum Press, 1973.

These protective groups are eliminated using the usual methods described for the selected protective group. In the case of elimination of *tert*-butoxycarbonyl, cleavage is usually done by acid hydrolysis.

Formula (I) compounds have shown potent activity with respect to β_3-adrenergic receptors. Furthermore, these compounds are not very toxic. Specifically, their acute toxicity is compatible with their use as drugs for the treatment of diseases where compounds with an affinity for the β_3 receptors are applicable.

The activity of the compounds of this invention relative to ###$_3$ [sic] activity has been shown using *in vitro* tests on the human colon according to the method described in EP-B-436435 and in T. Croci et al., Br. J. Pharmacol., 1997, 122: 139P.

More particularly, we have found that formula (I) compounds are much more active on the isolated colon than on the atrium and the trachea.

These surprising properties of formula (I) compounds make it possible to consider using them a drugs with ###$_3$ [sic] action.

Formula (I) compounds as well as their pharmaceutically acceptable salts may thus be indicated, for example, for the treatment of gastrointestinal diseases such as irritable bowel syndrome, as intestinal motricity modulators, as lipolytics, anti-obesity agents, antidiabetics, psychotropics, antiglaucoma agents, cicatrizants, antidepressants, as tocolytics to prevent or delay premature labor, and for treatment and/or prophylaxis of dysmenorrhea.

The above use of formula (I) compounds, as well as their pharmaceutically acceptable salts and solvates, for the preparation of the aforesaid drugs, constitutes a further aspect of this invention.

For such a use, in mammals requiring such treatment, an effective quantity of a formula (I) compound or one of its pharmaceutically acceptable salts or solvates is administered.

The above formula (I) compounds and their pharmaceutically acceptable salts or solvates may be used at daily doses of 0.01 to 20 mg per kg of body weight of the mammal to be treated, and, preferably, daily doses of 0.1 to 10 mg/kg. In humans, the dosage may vary, preferably from 0.5 mg to 1500 mg daily, particularly from 2.5 to 500 mg, depending on the subject to be treated, type of treatment (prophylactic or curative), and the severity of the condition. Formula (I) compounds are generally administered in dosage units of 0.1 to 500 mg, and preferably 0.5 to 100 mg of active ingredient, one to five times daily.

Said dosage units are preferably formulated in pharmaceutical compounds in which the active ingredient is mixed with a pharmaceutical excipient.

Thus, according to another of its aspects, this invention relates to pharmaceutical compounds that contain an aforesaid formula (I) compound or one of its pharmaceutically acceptable salts and solvates, as an active ingredient.

In the pharmaceutical compounds of this invention, for oral, sublingual, subcutaneous, intramuscular, intravenous, topical, transdermal, or rectal administration, the aforesaid formula (I) active ingredients, and their pharmaceutically acceptable salts and solvates, may be administered in unit dosage forms, in combination with standard pharmaceutical vehicles, to animals and humans, for treatment of the aforesaid conditions. The appropriate unit dosage forms include oral forms such as tablets, capsules, powders, granulates and oral solutions or suspensions, sublingual and buccal dosage forms, subcutaneous, intramuscular, or intravenous dosage forms, local dosage forms, and rectal dosage forms.

When preparing a solid compound in tablet form, the active ingredient is mixed with a pharmaceutical vehicle such as gelatin, starch, lactose, magnesium stearate, talc, gum arabic, etc. The tablets may be coated with sucrose or other appropriate substances, or processed such that they have extended or delayed activity and continuously release a predetermined quantity of active ingredient.

A capsule preparation is obtained by mixing the active ingredient with a diluent and pouring said mixture into soft or hard capsule shells.

A preparation in the form of a syrup or elixir may contain the active ingredient along with a sweetener (preferably non-caloric), methylparaben and propylparaben as antiseptics, as well as a flavoring agent and an appropriate colorant.

Water-dispersible powders and granulates may contain the active ingredient mixed with dispersion agents or wetting agents, or suspension agents such as polyvinylpyrrolidone, as well as with sweeteners or flavor enhancers.

Water-dispersible powders and granulates may contain the active ingredient mixed with dispersion agents or wetting agents, or suspension agents such as polyvinylpyrrolidone, as well as with sweeteners or flavor enhancers.

For local administration, the active ingredient is mixed with an excipient to prepare creams or unguents, or is dissolved in a vehicle for intraocular administration, for example, in the form of drops.

For rectal administration, suppositories are used, which are prepared with binders that melt at rectal temperature, for example, cocoa butter or polyethylene glycols.

For parenteral administration, aqueous solutions, saline solutions, or sterile and injectable solutions are used, which contain pharmacologically compatible dispersion agents and/or wetting agents, for example, propylene glycol or butylene glycol.

The active ingredient may also be formulated in microcapsule form, possibly with one or more vehicles or additives.

According to another of its aspects, this invention relates to a method of treating diseases that are improved by $###_3$-[sic] agonist action, which consists of administering a formula (I) compound or one of its pharmaceutically acceptable salts or solvates.

Formula (I) compounds, and particularly isotope-labeled formula (I) compounds, may also be used as laboratory tools for biochemical tests.

Formula (I) compounds bind to the $###_3$-[sic] adrenergic receptor. Therefore, these compounds may be used in an ordinary binding test using organ tissue where this receptor is particularly abundant, by measuring the quantity of formula (I) compound displaced by a test compound, in order to evaluate the affinity of said compound relative to the binding sites of that particular receptor.

Thus, another specific object of this invention is a reagent usable in biochemical tests that includes at least one appropriately labeled formula (I) compound.

The following examples illustrate the invention.

EXAMPLE 1

4-*tert*-butyoxycarbonyamino-piperidine.

At ambient temperature, mix for 2 hours 25 g (0.13 mol) of 4-amino-1-benzylpiperadine, 36.2ml (0.26 mol) of triethylamine, and 31.2 g (0.143 mol) of di-tert-butyl dicarbonate in 200 ml of dimethyl formamide. Pour the mixture into water, extract with ethyl acetate, wash with water, and crystallize the product obtained in 200 ml isopropyl ether. This produces 33 g of 1-benzyl-4-tert-butoxycarbonylamino-

piperidine. Hydrogenate in a mixture of 200 ml of ethanol and 100 ml of tetrahydrofuran in the presence of 3 g of 10% Pd/C. After filtering the catalyst, isolate the above-referenced compound. MP 157-160°C.

EXAMPLE 2

4-*tert*-butoxycarbonylamino-1-(5-ethoxycarbonylpyrid-2-yl)-piperidine.

Heat at 80°C for 18 hours a mixture of the product from Example 1, triethylamine, and 6-chloronicotinic acid. After cooling, add water, extract with ethyl acetate, dry the organic phase on sodium sulfate, and evaporate the solvent under reduced pressure. This results in the above-referenced compound. MP 140-142°C.

EXAMPLE 3

4-amino-1-(5-ethoxycarbonylpyrid-2-yl)-piperidine (hydrated dihydrochloride).

Dissolve the product from Example 2 in ethyl acetate and add a 3N solution of hydrochloric acid in ethyl acetate and stir at ambient temperature for 10 hours. Filter and wash with acetone. This results in the above-referenced compound. MP 148-150°C.

EXAMPLE 4

2-amino-3-nitro-1-(2,3-epoxypropoxy)-benzene.

Mix 21.7 g (0.0095 mol) of glycidyl tosylate, 10 g (0.0475 mol) of 2-amino-3-nitrophenol, 6.5 g of K_2CO_3 grated into acetone, and heat to reflux for 18 hours. Filter and evaporate the solvent under reduced pressure. Purify the crude product by flash chromatography, by eluting with a 9:1 mixture of hexane/ethyl acetate. This results in the above-referenced compound. MP 76-78°C.

EXAMPLE 5

3-[1-(5-ethoxycarbonylpyrid-2-yl)-piperidinylamino]-1-(2-amino-3-nitrophenoxy)-2-propanol.

Mix 1 g (0.00475 mol) of the compound from the previous step with 1.53 g (0.00475 mol) of 4-amino-1-(5-ethoxycarbonylpyrid-2-yl)-piperidine in 50 ml of ethanol. Heat to reflux overnight and evaporate under reduced pressure. Purify the crude product by flash chromatography, by eluting with a 9:1 mixture of ethyl acetate/ethanol. This results in the above-referenced compound. MP 140-142°C.

EXAMPLE 6

3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-(2,3 diaminophenoxy)-2-propanol.

Hydrogenate 1.71 g (0.0037 mol) of the compound from the previous step at ambient temperature in 120 ml of ethanol in the presence of 0.8 g of 5% Pd/C. After filtering and evaporating the solvent, purify

the crude product by flash chromatography, by eluting with a 7:3 mixture of ethyl acetate/ethanol. This results in the above-referenced compound.

EXAMPLE 7

3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[1,2-dihydro-2-oxo-benzimidazole-4-yloxyl]-2-propanol.

Stir the product from the previous step at ambient temperature overnight with 0.44 g of N,N-carbonyl diimidazole (0.027 mol) in 50 ml of THF. Evaporate the solvent under reduced pressure, add ethyl acetate, and wash with water. After dehydrating and evaporating the solvent, purify by chromatography a first time, by eluting with an 8:2 mixture of ethylene chloride/methanol, and a second time, by eluting with an 8:2 mixture of methanol/ethyl acetate. This results in the above-referenced compound. MP 191-193°C.

EXAMPLE 8

2-[2-(4-nitrophenyl)-diazenyl]-5-(2,3-epoxypropoxy)-pyridine.

To a solution containing 1.82 g of 5-hydroxy-2-(2-(4-nitrophenyl)diazenyl)pyridine (0.01043 mol) prepared according to the procedure described in J. Am. Chem. Soc., 1959, 81, 6049, 0.692 ml of 2,3-epoxypropanol (0.01043 mol) and 2.74 g of Ph_3P (0.01043 mol) in 18 ml of DMF, add at 0°C, under a nitrogen atmosphere, 1.64 ml of diethylazodicarboxylate (0.01043 mol). Let react for one hour at 0°C and then for 40 hours at ambient temperature while stirring. Add water, extract with ethyl acetate, wash, and evaporate the solvent. Purify the crude product by eluting with an 100:2 mixture of CH_2Cl_2/CH_3OH. This results in the above-referenced compound. MP 150-152°C (dec.).

EXAMPLE 9

3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[2-(2-(4-nitrophenyl)-diazenyl)-pyrid-5-yloxyl]-2-propanol.

Heat to reflux for 7 hours a solution of 1.15 g (0.00383 mol) of the product from Example 8 and 1.05 g (0.00421 mol) of 1-(5-ethoxycarbonypyrid-2-yl)-4-piperidylamino in 20 ml of ethanol. Filter, dry, and crystallize in a solution of ethanol and CH_2Cl_2. This results in the above-referenced compound. MP 172°C.

EXAMPLE 10

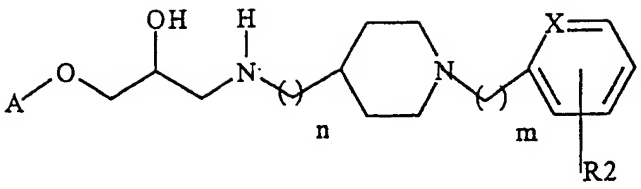
3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[2-amino-pyrid-5-yloxyl]-2-propanol.

Dissolve 1.37 g (0.002509 mol) of the product from Example 9 with 0.16 g of Pd/C in 30 ml of ethanol and 2 ml of CH_3COOH (d = 1.049, 0.0347 mol). Hydrogenate for 9 hours while stirring at a temperature between 15 and 20°C. Filter the crude product on celite and wash with ethanol. Evaporate the solvent and

add 30 ml of a saturated solution of $NaHCO_3$, and 5 ml 1N NaOH, and extract with ethyl acetate. Evaporate the solvent and purify the crude product by chromatography, by eluting with a 95:5:0.5 and then a 90:10:1 mixture of $CH_2Cl_2/CH_3OH/NH_4OH$. This results in the above-referenced compound. MP 120-122°C.

CLAIMS

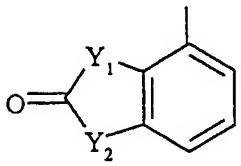
1. Formula (I) compound:



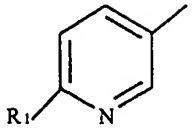
(I)

where X is N or CH

A represents a group with formula (a) or (b)



(a)



(b)

R_1 represents hydrogen or a $-NH_2$, $-NR_3R_4$, $-NR_3CO(C_1-C_4)$ $Alk_5-NR_3SO_2(C_1-C_4)Alk$ group

R_2 represents hydrogen or a $(C_1-C_4)Alk$ group, a (C_1-C_4)alkoxyl group, a halogen, $-COOH$, $-COO(C_1-C_4)Alk$, $-CN$, $-CONR_3R_4$, $-NO_2$, $-SO_2NR_3R_4$, $-NHSO_2(C_1-C_4)Alk$

m and n independently represent 0, 1, or 2

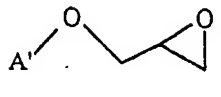
R_3 and R_4 independently represent hydrogen or a $(C_1-C_4)Alk$ group

Y_1 and Y_2 independently represent NH or O

and their salts or solvates.

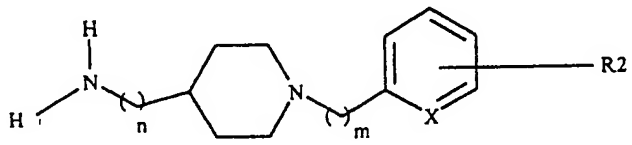
2. Compounds according to Claim 1, where X represents CH.
3. Compounds according to Claim 1, where X represents nitrogen and the R_2 group is in position 5.
4. Compounds according to Claim 1, where the $(C_1-C_4)Alk$ group is a methyl or ethyl group.
5. Compounds according to Claim 1, where R_2 is one of the following: $-COOH$, $-COO(C_1-C_4)Alk$, $-CN$, NO_2, $-CONR_3R_4$, or $-NHSO_2-(C_1-C_4)Alk$.
6. 3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[1,2-dihydro-2-oxo-benzimidazol-4-yloxy]-2]-propanol and its salts or solvates.
7. 3-[1-(5-ethoxycarbonylpyrid-2-yl)-4-piperidinylamino]-1-[2-amino-pyrid-5-yloxy]-2-propanol and its salts or solvates.

8. Process for preparing the compounds from Claim 1, wherein a formula (II) epoxy:



(II)

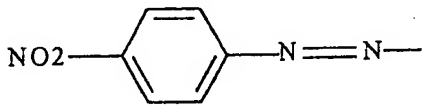
where A' represents the (a) group or the (b) group, in which R_1 is possibly protected by a protective group, where (a), (b), and R_1 are as specified in Claim 1, is reacted with a formula (III) amine



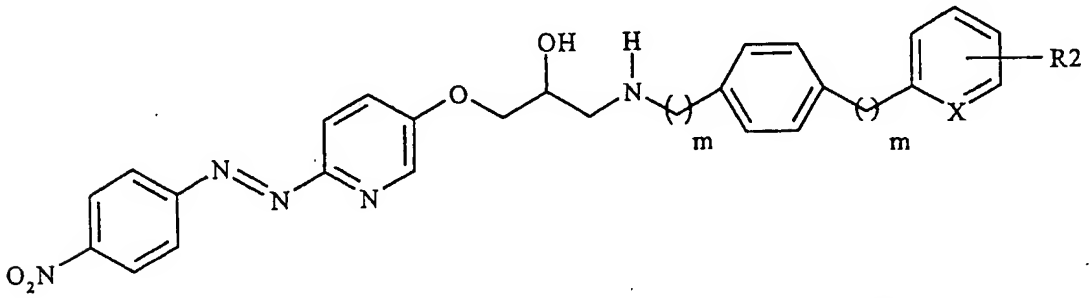
(III)

where m, n, R_2, and X are as indicated above, while eliminating the protective group that is possibly present and transforming the formula (I) product thus obtained into one of its salts or solvates.

9. Process for preparing the compounds from Claim 1, where A represents a (b) group and R_1 is an NH_2 group, wherein a formula (II) product, as specified in Claim 8, where A' is the (b) group and R_1 is a group with the formula:



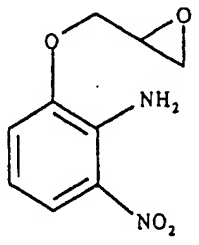
is reacted with a formula III amine, and the formula IV product thus obtained:



(IV)

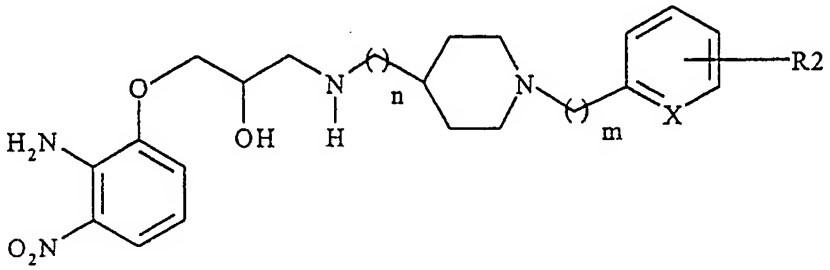
is subjected to a hydrogenation reaction to transform the 4-nitrophenyldiazenyle group into an amino group and the formula (I) product thus obtained may possibly be transformed into one of its salts or solvates.

10. Process for preparing the compounds from Claim 1, where A represents the (a) group and Y_1 and Y_2 represent a nitrogen atom, wherein a formula (V) compound:



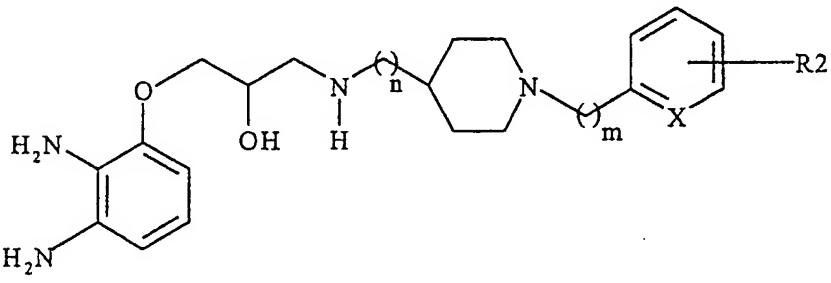
(V)

is reacted with a formula (III) compound as specified in Claim 8, the nitro group from the formula (VI) product thus obtained:



(VI)

is reduced, the formula (VII) product thus obtained:



(VII)

is processed with a carbonylation agent, the formula (I) product thus obtained is isolated, and may possibly be transformed into one of its salts or solvates.

11. Process according to Claim 10, wherein the carbonylation agent is either carbonyl diimidazole or carbonyl chloride.

12. Pharmaceutical compound comprising at least one compound from Claim 1 as its active ingredient.

13. Use of a compound according to Claim 1 for the preparation of drugs used in irritable bowel syndrome, as intestinal motricity modulators, as lipolytics, anti-obesity agents, antidiabetics,

psychotropics, antiglaucoma agents, cicatrizants, antidepressants, as tocolytics to prevent or delay premature labor, and for treatment and/or prophylaxis of dysmenorrhea.